

## Supporting Information

# A Versatile Fluorescence Approach for Kinetic and Mechanistic Studies of Hydrocarbon Autoxidations and their Inhibition by Radical-Trapping Antioxidants

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## Table of Contents

<b>Autoxidation of 7-Dehydrocholesterol and its Inhibition by PMHC.....</b>	<b>S2</b>
<b>Autoxidation of Hexadecane and its Inhibition by BHT.....</b>	<b>S2</b>
<b>Derivation of Second Order Rate Constants for Reaction of 7 with tetralin hydroperoxide.....</b>	<b>S3</b>
<b>Synthesis of Coumarin-Triarylphosphine Conjugates 4-7 and their Corresponding Oxides.....</b>	<b>S6</b>
<b>NMR Spectra.....</b>	<b>S10</b>
<b>References.....</b>	<b>S29</b>

### **Autoxidation of 7-Dehydrocholesterol and its Inhibition by PMHC**

7-Dehydrocholesterol (7-DHC) was recrystallized from methanol and passed through a short silica plug (3:1 hexanes:EtOAc) immediately before use. Pure 7-DHC was dissolved in 1,2-dichlorobenzene (chosen to minimize solvent evaporation in open microplate wells) and a solution of it, the azo initiator MeOAMVN (also known as V-70), and 2,2,5,7,8-pentamethyl-6-hydroxychroman (PMHC) were added to the wells of a 96-well microplate (the final concentrations were  $[7\text{-DHC}] = 78 \text{ mM}$ ,  $[\text{PMHC}] = 4 \text{ }\mu\text{M}$  and  $[\text{MeOAMVN}] = 20 \text{ }\mu\text{M}$  in a total volume of  $25 \text{ }\mu\text{L}$ ). The plate was brought to  $37 \text{ }^\circ\text{C}$  in the thermostatted chamber of a microplate reader, and a well was quenched every 5 minutes by dilution with  $205 \text{ }\mu\text{L}$  methanol, followed by addition of  $25 \text{ }\mu\text{L}$  of **7** ( $20 \text{ }\mu\text{M}$  final concentration) as a solution in acetonitrile (which also contained  $50 \text{ mM}$  BHT). Both solutions were added directly to the microplate wells by the automated dual reagent dispenser designed for use with our microplate reader. The fluorescence was then measured every 2 seconds for 1 minute (excitation:  $340 \text{ nm}$ , emission:  $425 \text{ nm}$ ) to obtain the initial rate, from which the hydroperoxide concentration could be determined.

### **Autoxidation of Hexadecane and its Inhibition by BHT**

Hexadecane, which was purified by passage through silica, was warmed to  $160 \text{ }^\circ\text{C}$  in a stirred flow reactor under continuous flow of nitrogen. Once equilibrated, tetralin hydroperoxide ( $10 \text{ mM}$ ) was added and the nitrogen atmosphere was replaced with an oxygen atmosphere, again, under continuous flow. Samples were removed at regular intervals and cooled to room temperature. A small volume ( $30 \text{ }\mu\text{L}$ ) of each sample was

loaded into the wells of a 96-well microplate, and the fluorescence of each well was then measured at 25 °C every 2 seconds for 1 minute (excitation: 340 nm, emission: 425 nm) following addition of 200 µL of *t*-amyl alcohol and 20 µL of **7** (20 µM final concentration) as a solution in acetonitrile (which also contained 50 mM BHT).

### **Derivation of Second Order Rate Constants for Reaction of **7** with tetralin hydroperoxide**

The kinetics of the reaction of a hydroperoxide and a triarylphosphine (given as **7**) in a protic solvent are given by:<sup>1</sup>

$$v = d[\text{ROOH}]/dt = k[\mathbf{7}][\text{ROOH}] \quad (\text{S1})$$

For reactions carried out at constant  $[\mathbf{7}]$ , but varying  $[\text{ROOH}]$  a plot of the initial rate ( $v_0$ ) versus  $[\text{ROOH}]_0$  should be linear with a slope corresponding to the pseudo first order rate constant  $k' = k[\mathbf{7}]$ . In Figure 1 of the manuscript are plotted the initial rates for the reactions of **7** with varying  $[\text{ROOH}]$  in methanol at 37°C and in *t*-amyl alcohol at 25°C. The initial rates are obtained from data shown in Figures S1 and S2 (the five representative data sets are shown for each), which represent the change in concentration of **11** (the oxidized form of **7**) as a function of time for different  $[\text{ROOH}]$ . The concentration of **11** is obtained as follows:

$$\text{total counts} = \text{response factor for } \mathbf{11} \times [\mathbf{11}] + \text{response factor for } \mathbf{7} \times [\mathbf{7}] \quad (\text{S1})$$

The response factors are dependent on the particular instrument and specific operating parameters, and are obtained from a standard curve of counts as a function of the

authentic material. In our case, such standard curves for **11** in methanol and *t*-amyl alcohol yield response factors of 6000 and 8600 counts/ $\mu\text{M}$ , respectively. The corresponding response factors for **7** are 566 and 811 counts/ $\mu\text{M}$ , respectively. Since, in our experiments  $[\mathbf{11}] + [\mathbf{7}] = 20 \mu\text{M}$ , Eq. S1 becomes:

$$\begin{aligned} \text{total counts} &= \text{response factor for } \mathbf{11} \times [\mathbf{11}] + \text{response factor for } \mathbf{7} \times (20 \mu\text{M}) \\ &\quad - \text{response factor for } \mathbf{7} \times [\mathbf{11}] \end{aligned} \quad (\text{S2})$$

which, in methanol at 37°C, gives:

$$\text{total counts} = 5434 \times [\mathbf{11}] + 11320 \quad (\text{S3})$$

and, in *t*-amyl alcohol at 25°C, gives:

$$\text{total counts} = 7789 \times [\mathbf{11}] + 16220 \quad (\text{S4})$$

which are used to obtain the initial rates from the fluorescence counts obtained as a function of time.

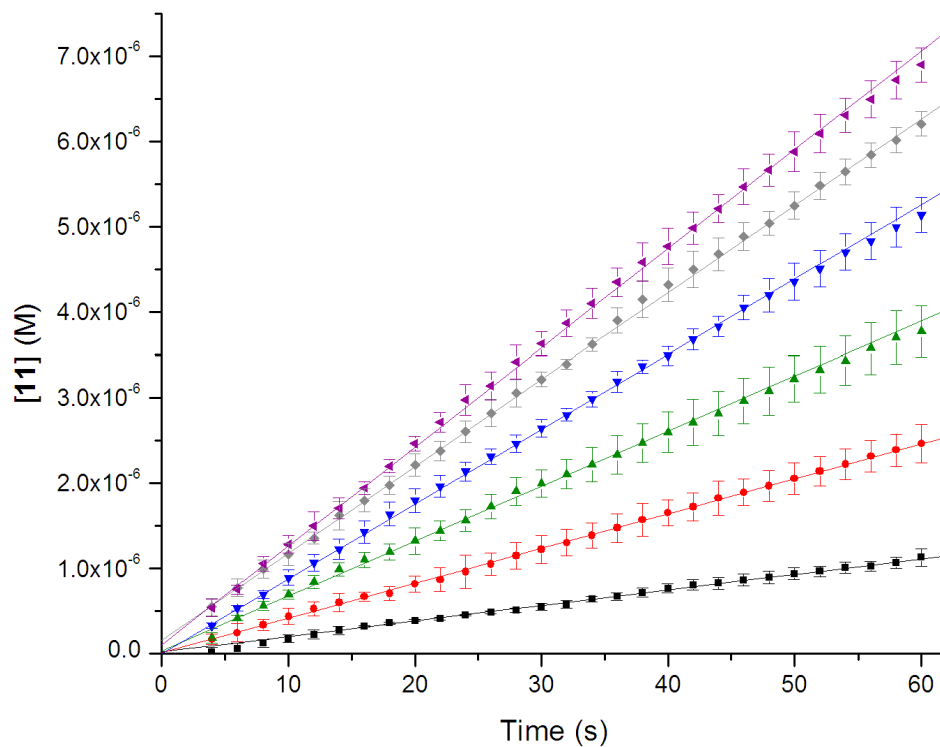
The slopes of the lines in Figure 1 provide the pseudo-first order rate constants for the reaction of  $k' = k[\mathbf{7}]$ , and therefore

*in methanol at 37°C:*

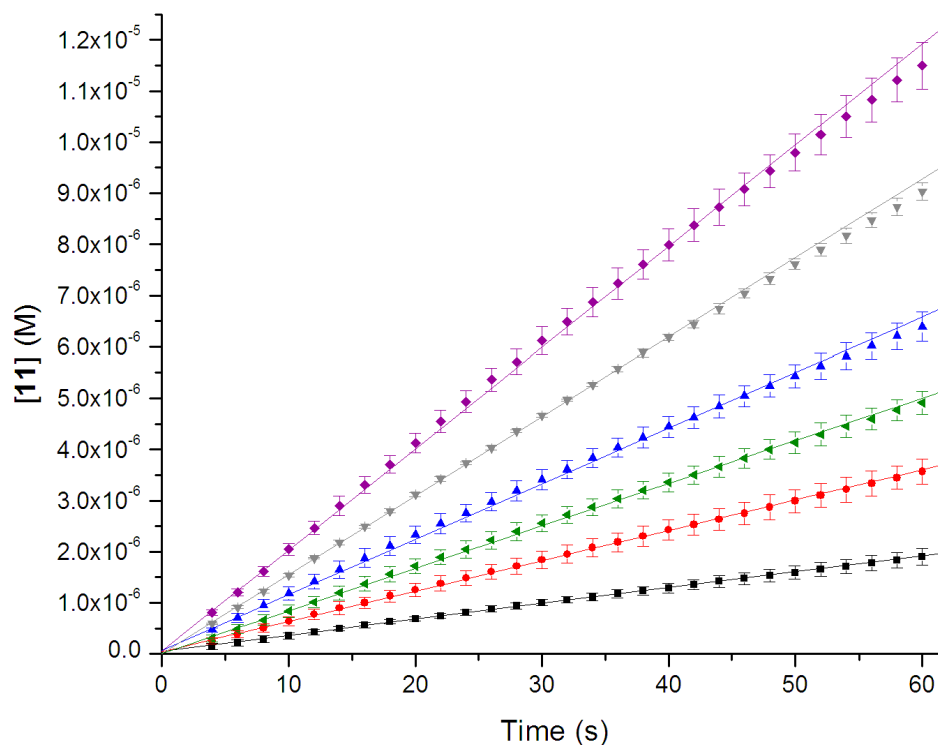
$$k = k'/[\mathbf{7}] = 1.8 \times 10^{-4} \text{ s}^{-1} / 2 \times 10^{-5} \text{ M} = 9.1 \text{ M}^{-1} \text{ s}^{-1}$$

*in t-amyl alcohol at 25°C:*

$$k = k'/[\mathbf{7}] = 2.4 \times 10^{-5} \text{ s}^{-1} / 2 \times 10^{-5} \text{ M} = 1.2 \text{ M}^{-1} \text{ s}^{-1}$$



**Figure S1.** Formation of **11** as a function of time from reaction of **7** with various concentrations (100, 200, 300, 400, 500 and 600 μM) of tetralin hydroperoxide in methanol at 37°C.



**Figure S2.** Formation of **11** as a function of time from reaction of **7** with various concentrations (600, 1200, 1800, 2400, 3600 and 4800  $\mu\text{M}$ ) of tetralin hydroperoxide in *t*-amyl alcohol at 25°C.

### Synthesis of Coumarin-Triarylphosphine Conjugates **4-7** and their Corresponding Oxides

**7-(Diethylamino)-3-(4-iodophenyl)-2H-chromen-2-one.** A solution of 4-iodophenylacetonitrile<sup>2</sup> (4.33 g, 17.8 mmol), *p*-(diethylamino)salicylaldehyde (3.38 g, 17.5 mmol) and piperidine (1.52 g, 17.8 mmol) in 35 mL EtOH was heated to reflux until reaction completion, determined by TLC. The reaction was quenched by addition to 150 mL H<sub>2</sub>O and extracted 3x with EtOAc. Organics were washed with brine and dried over MgSO<sub>4</sub> to afford a red oil. Purification by column chromatography (EtOAc/Hexanes 1:4) to obtain a yellow solid. Yield: 72 % green solid. <sup>1</sup>H NMR (CDCl<sub>3</sub>, 400 MHz)  $\delta$  ppm 7.72-7.69 (m, 2H), 7.67 (s, 1H), 7.46-7.42 (m, 2H), 7.29 (d,  $J = 8.0$  Hz, 1H), 6.58 (dd,  $J =$

8.8, 2.4 Hz, 1H), 6.49 (d,  $J = 2.4$  Hz, 1H), 3.41 (q,  $J = 7.1$  Hz, 4H), 1.21 (t,  $J = 7.1$  Hz, 6H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  ppm 161.224, 156.209, 150.653, 140.504, 137.276, 135.269, 129.897, 129.022, 119.302, 109.007, 108.826, 96.935, 93.222, 44.811, 12.414. HRMS (EI)  $m/z$  calculated 419.0382, found 419.0369.

**3-(4-Iodophenyl)-7-methoxy-2H-chromen-2-one.** A solution of 4-iodophenylacetonitrile<sup>2</sup> (4.33 g, 17.8 mmol), 2-hydroxy-4-methoxybenzaldehyde<sup>3</sup> (3.38 g, 17.5 mmol) and piperidine (1.52 g, 17.8 mmol) in 35 mL EtOH was heated to reflux until reaction completion, determined by TLC. The reaction was quenched by addition to 150 mL  $\text{H}_2\text{O}$  and extracted 3x with EtOAc. Organics were washed with brine and dried over  $\text{MgSO}_4$  to afford a red oil. Purification by column chromatography (EtOAc/Hexanes 1:4) to obtain a peach-coloured solid. Yield: 67% brown solid.  $^1\text{H}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 400 MHz)  $\delta$  ppm 8.13 (s, 1H), 7.81 (d,  $J = 8.5$  Hz, 2H), 7.66 (d,  $J = 8.5$  Hz, 1H), 7.58 (d,  $J = 8.5$  Hz, 2H), 6.98-6.93 (m, 2H), 3.94 (s, 3H).  $^{13}\text{C}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 100 MHz)  $\delta$  ppm 165.013, 161.516, 157.434, 142.405, 139.172, 137.046, 132.292, 131.517, 124.830, 115.136, 114.550, 102.019, 95.286, 57.394. HRMS (EI)  $m/z$  calculated 377.9753, found 377.9767.

### General procedure for coupling to give 4-7

To a solution of aryl iodide (4.0 mmol) in 4.0 mL  $N,N$ -dimethylacetamide (freshly distilled over BaO) was added  $\text{Pd}(\text{OAc})_2$  (2 mg, 4  $\mu\text{mol}$ ), KOAc (471 mg, 4.8 mmol) and  $\text{Ar}_2\text{PH}$  (781 mg, 4.2 mmol). The reaction was stirred at 100 °C until completion, as determined by TLC. Quenched by addition to  $\text{H}_2\text{O}$  and extraction with  $\text{CH}_2\text{Cl}_2$ . Washed with brine and dried over  $\text{MgSO}_4$ . Purified by column chromatography, eluting with EtOAc/Hexanes, followed by recrystallization to analytical purity.

**7-(Diethylamino)-3-(4-(diphenylphosphino)phenyl)-2H-chromen-2-one (4).** Yield: 60% yellow powder.  $^1\text{H}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 400 MHz)  $\delta$  ppm 8.01 (s, 1H), 7.78 (dd,  $J = 8.4$ , 1.2 Hz, 2H), 7.48 (d,  $J = 9.0$  Hz, 1H), 7.42-7.30 (m, 12H), 6.75 (dd,  $J = 8.8$ , 2.4 Hz, 1H), 6.64 (d,  $J = 2.4$  Hz, 1H), 3.52 (q,  $J = 7.0$  Hz, 4H), 1.22 (t,  $J = 7.0$  Hz, 6H).  $^{13}\text{C}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 100 MHz)  $\delta$  ppm 162.225, 158.321, 152.833, 142.811, 139.250, 139.134, 138.673, 135.515, 135.319, 135.237, 135.040, 131.438, 130.743, 130.548, 130.479,

130.123, 130.054, 121.050, 110.983, 110.736, 98.308, 46.291, 13.744. HRMS (EI)  $m/z$  calculated 477.1858, found 477.1879.

**3-(4-(Di-*p*-tolylphosphino)phenyl)-7-(diethylamino)-2H-chromen-2-one (5).** Yield: 77% yellow solid.  $^1\text{H}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 300 MHz)  $\delta$  ppm 7.99 (s, 1H), 7.75 (dd,  $J = 8.5$ , 1.3 Hz, 2H), 7.47 (d,  $J = 9.0$  Hz, 1H), 7.32-7.25 (m, 2H), 7.23-7.22 (m, 8H), 6.74 (dd,  $J = 9.0$ , 2.4 Hz, 1H), 6.53 (d,  $J = 2.4$  Hz, 1H), 3.52 (q,  $J = 7.0$  Hz, 4H), 2.34 (s, 6H), 1.22 (t,  $J = 7.0$  Hz, 6H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  ppm 161.387, 156.102, 150.486, 140.518, 138.559, 137.287, 137.176, 135.811, 133.778, 133.695, 133.582, 133.370, 133.179, 129.227, 129.155, 128.922, 127.949, 127.882, 119.967, 108.910, 96.892, 44.792, 21.191, 12.354. HRMS (EI)  $m/z$  calculated 505.2171, found 505.2194.

**3-(4-(Diphenylphosphino)phenyl)-7-methoxy-2H-chromen-2-one (6).** Yield: 80% yellow solid.  $^1\text{H}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 400 MHz)  $\delta$  ppm 8.09 (s, 1H), 7.76 (d,  $J = 7.1$  Hz, 2H), 7.62 (d,  $J = 8.4$  Hz, 1H), 7.40-7.31 (m, 12H), 6.95-6.91 (m, 2H), 3.92 (s, 3H).  $^{13}\text{C}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 100 MHz)  $\delta$  ppm 164.861, 161.602, 157.334, 142.399, 139.388, 139.266, 139.038, 138.923, 137.791, 135.538, 135.341, 135.201, 135.005, 131.411, 130.794, 130.559, 130.489, 130.395, 130.327, 125.233, 115.137, 114.464, 101.940, 57.341. HRMS (EI)  $m/z$  calculated 436.1228, found 436.1243.

**3-(4-(Di-*p*-tolylphosphino)phenyl)-7-methoxy-2H-chromen-2-one (7).** Yield: 85% off-white solid.  $^1\text{H}$  NMR ( $(\text{CD}_3)_2\text{CO}$ , 400 MHz)  $\delta$  ppm 8.12 (s, 1H), 7.76 (d,  $J = 8.0$  Hz, 2H), 7.65 (d,  $J = 8.4$  Hz, 1H), 7.32 (m, 2H), 7.23 (m, 8H), 6.94 (m, 2H), 3.94 (s, 3H), 2.34 (s, 6H).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz)  $\delta$  ppm 164.913, 161.660, 157.338, 142.334, 140.745, 137.559, 135.768, 135.644, 135.444, 134.971, 134.779, 131.434, 131.277, 131.205, 130.304, 130.238, 125.410, 115.218, 114.488, 102.003, 57.376, 22.260. HRMS (EI)  $m/z$  calculated 464.1541, found 464.1540.

### General procedure for oxidation to give 8-11

To a solution of phosphine dye (1.0 mmol) in 5 mL MeOH was added *tert*-butylhydroperoxide (1.0 mmol) at room temperature. Once oxidation was complete, the phosphine oxide was passed through a small silica column eluting with EtOAc, followed by recrystallization to analytical purity.



**7-(Diethylamino)-3-(4-(diphenylphosphoryl)phenyl)-2H-chromen-2-one (8).** Yield: 90% bright yellow solid. <sup>1</sup>H NMR ((CD<sub>3</sub>)<sub>2</sub>SO, 400 MHz) δ ppm 8.19 (s, 1H), 7.88 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.67-7.59 (m, 13H), 7.91 (d, *J* = 8.8 Hz, 1H), 6.74 (dd, *J* = 8.0, 2.0 Hz, 1H), 6.56 (d, *J* = 2.0 Hz, 1H), 3.44 (q, *J* = 6.8 Hz, 4H), 1.13 (t, *J* = 6.8 Hz, 6H). <sup>13</sup>C NMR ((CD<sub>3</sub>)<sub>2</sub>SO, 100 MHz) δ ppm 160.138, 155.983, 150.761, 142.258, 139.161, 133.210, 132.191, 131.974, 131.677, 131.447, 131.350, 131.315, 131.215, 130.649, 129.913, 128.750, 128.633, 128.017, 127.899, 117.197, 109.242, 108.231, 95.993, 44.065, 12.251. HRMS (ESI) *m/z* calculated 493.1807, found 493.1805.

**3-(4-(di-*p*-tolylphosphoryl)phenyl)-7-(diethylamino)-2H-chromen-2-one (9).** Yield: 56% yellow solid. <sup>1</sup>H NMR (*d*<sub>6</sub>-DMSO, 400 MHz) δ ppm 8.17 (s, 1H), 7.86 (dd, *J* = 8.0, 2.0 Hz, 2H), 7.61 (dd, *J* = 11.3, 8.4 Hz, 2H), 7.53-7.48 (m, 5H), 7.37-7.34 (m, 4H), 6.72 (dd, *J* = 8.8, 2.4 Hz, 2H), 6.55 (d, *J* = 2.0 Hz, 1H), 3.43 (q, *J* = 7.0 Hz, 4H), 2.36 (s, 6H), 1.12 (t, *J* = 7.0 Hz, 6H). <sup>13</sup>C NMR (*d*<sub>6</sub>-DMSO, 100 MHz) δ ppm 160.131, 155.961, 150.726, 142.167, 141.900 (d, *J* = 2.6 Hz), 138.924 (d, *J* = 2.6 Hz), 132.408, 131.475, 131.341, 131.245, 131.113, 130.399, 129.883, 129.297, 129.136, 129.008, 127.942, 127.786, 117.261, 109.214, 108.227, 95.983, 44.054, 21.007, 12.241. HRMS (EI) *m/z* calculated 521.2120, found 521.2123.

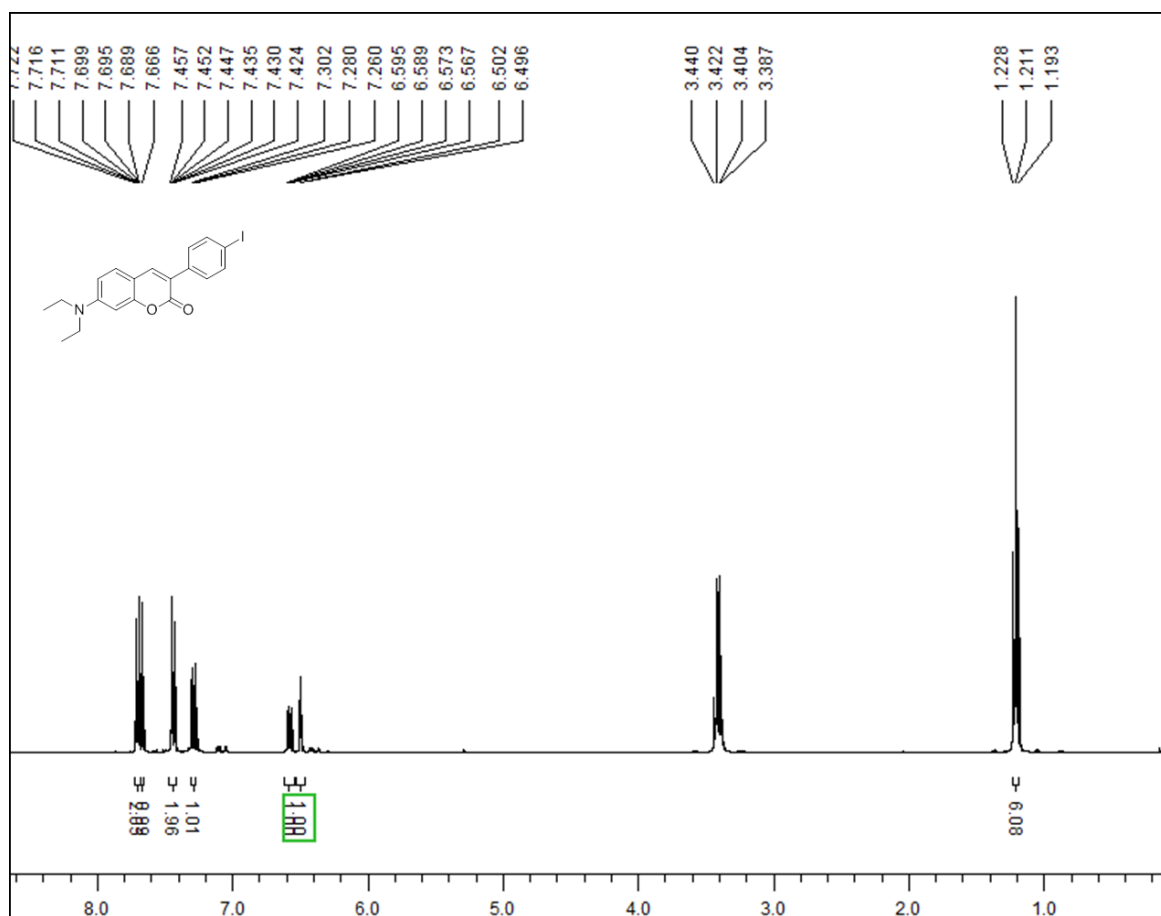
**3-(4-(Diphenylphosphoryl)phenyl)-7-methoxy-2H-chromen-2-one (10).** Yield: 92% pale-yellow solid. <sup>1</sup>H NMR ((CD<sub>3</sub>)<sub>2</sub>SO, 400 MHz) δ ppm 8.32 (s, 1H), 7.88 (d, *J* = 6.8 Hz, 2H), 7.72-7.57 (m, 14H), 7.05 (s, 1H), 6.99 (d, *J* = 8.6 Hz, 1H), 3.87 (s, 3H). <sup>13</sup>C NMR ((CD<sub>3</sub>)<sub>2</sub>CO, 100 MHz) δ ppm 165.168, 161.529, 157.561, 143.351, 140.805, 140.775, 135.968, 135.634, 134.945, 134.611, 133.735, 133.708, 133.612, 133.571, 133.473, 131.676, 130.511, 130.392, 130.259, 124.819, 115.081, 114.615, 102.007, 57.407. HRMS (EI) *m/z* calculated 452.1177, found 452.1182.

**3-(4-(Di-*p*-tolylphosphoryl)phenyl)-7-methoxy-2H-chromen-2-one (11).** Yield: 88% white solid. <sup>1</sup>H NMR ((CD<sub>3</sub>)<sub>2</sub>CO, 400 MHz) δ ppm 8.20 (s, 1H), 7.91 (dd, *J* = 8.1, 2.0 Hz, 2H), 7.76-7.67 (m, 3H), 7.61 (d, *J* = 8.0 Hz, 2H), 7.58 (d, *J* = 8.0 Hz, 2H), 7.37-7.35 (m, 4H), 6.95-6.96 (m, 2H), 3.95 (s, 3H), 2.41 (s, 6H). <sup>13</sup>C NMR (CDCl<sub>3</sub>, 100 MHz) δ ppm 165.148, 161.541, 157.547, 144.100 (d, *J* = 2.8 Hz), 143.283, 140.600 (d, *J* = 2.8 Hz), 136.120, 135.097, 133.750, 133.651, 133.518, 133.421, 132.875, 131.828, 131.656,

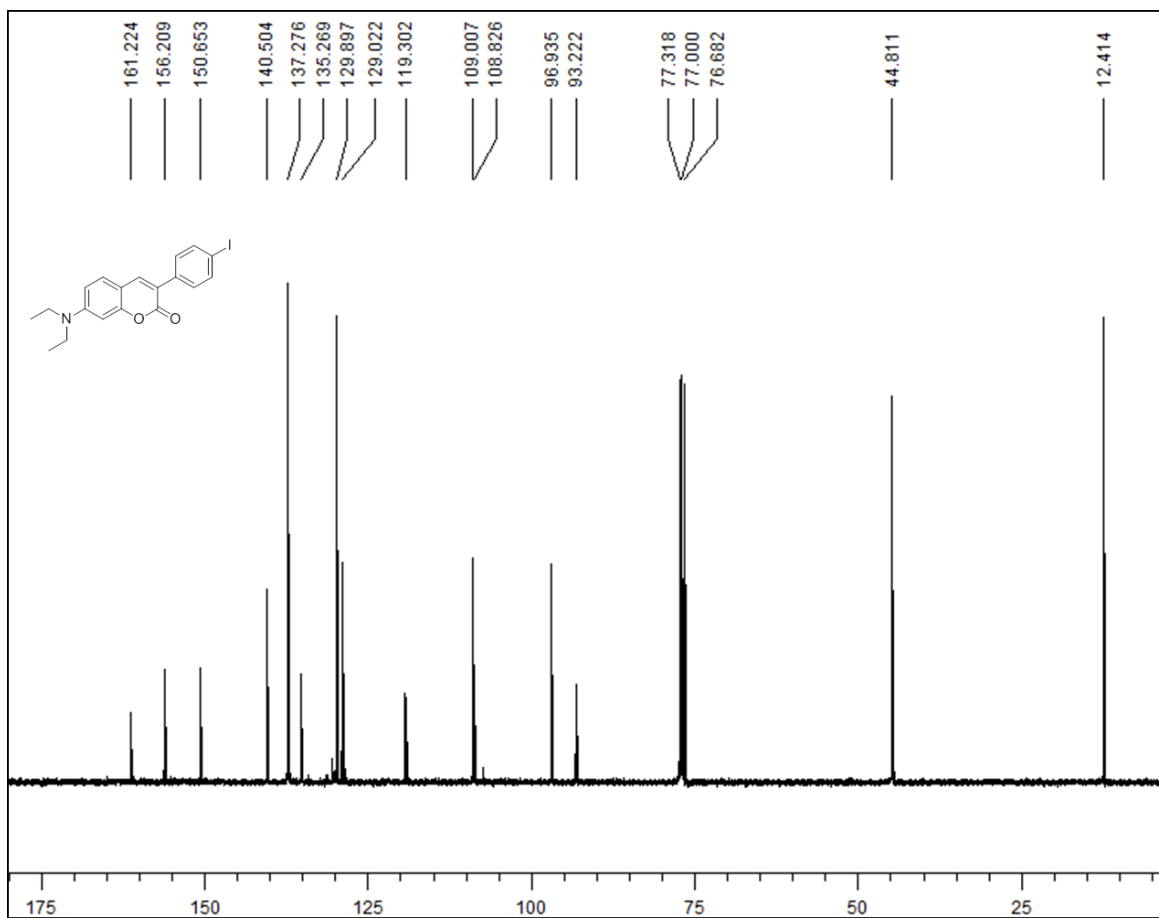
131.111, 130.989, 130.285, 130.167, 124.873, 115.087, 114.603, 102.003, 57.404, 22.500. HRMS (EI)  $m/z$  calculated 480.1490, found 480.1474.

## NMR Spectra

### 7-(Diethylamino)-3-(4-iodophenyl)-2H-chromen-2-one

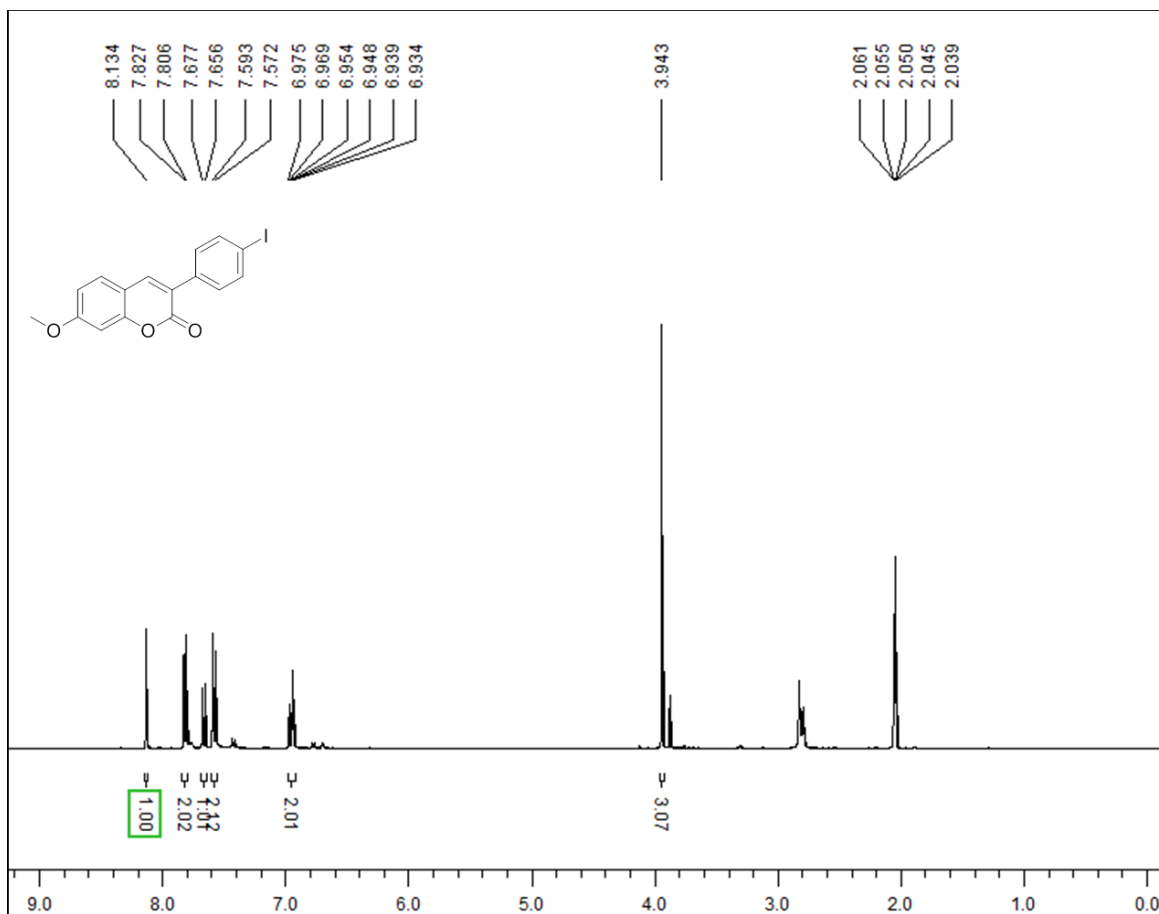


Note: Some reduced (deiodinated) material remains and was not purified further.



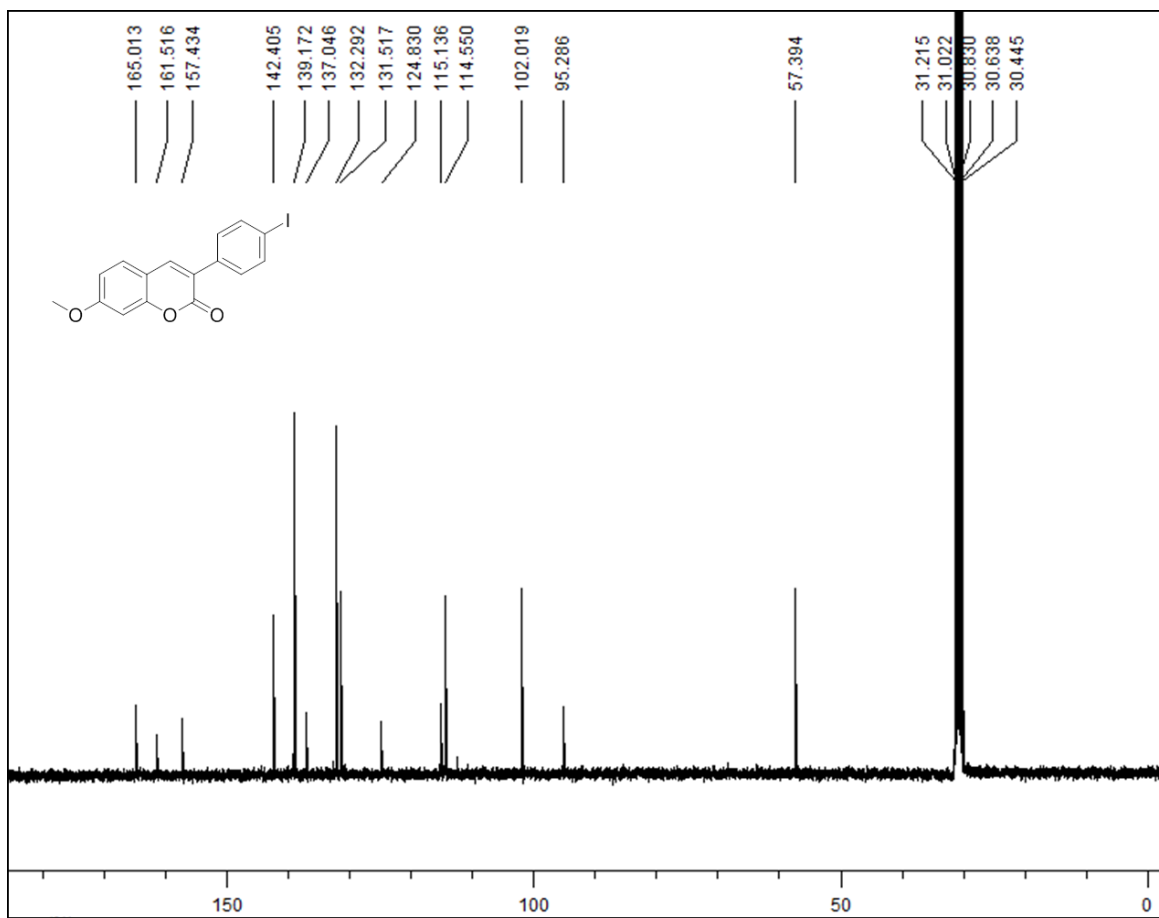
Note: Some reduced (deiodinated) material remains and was not purified further.

**3-(4-Iodophenyl)-7-methoxy-2H-chromen-2-one.**



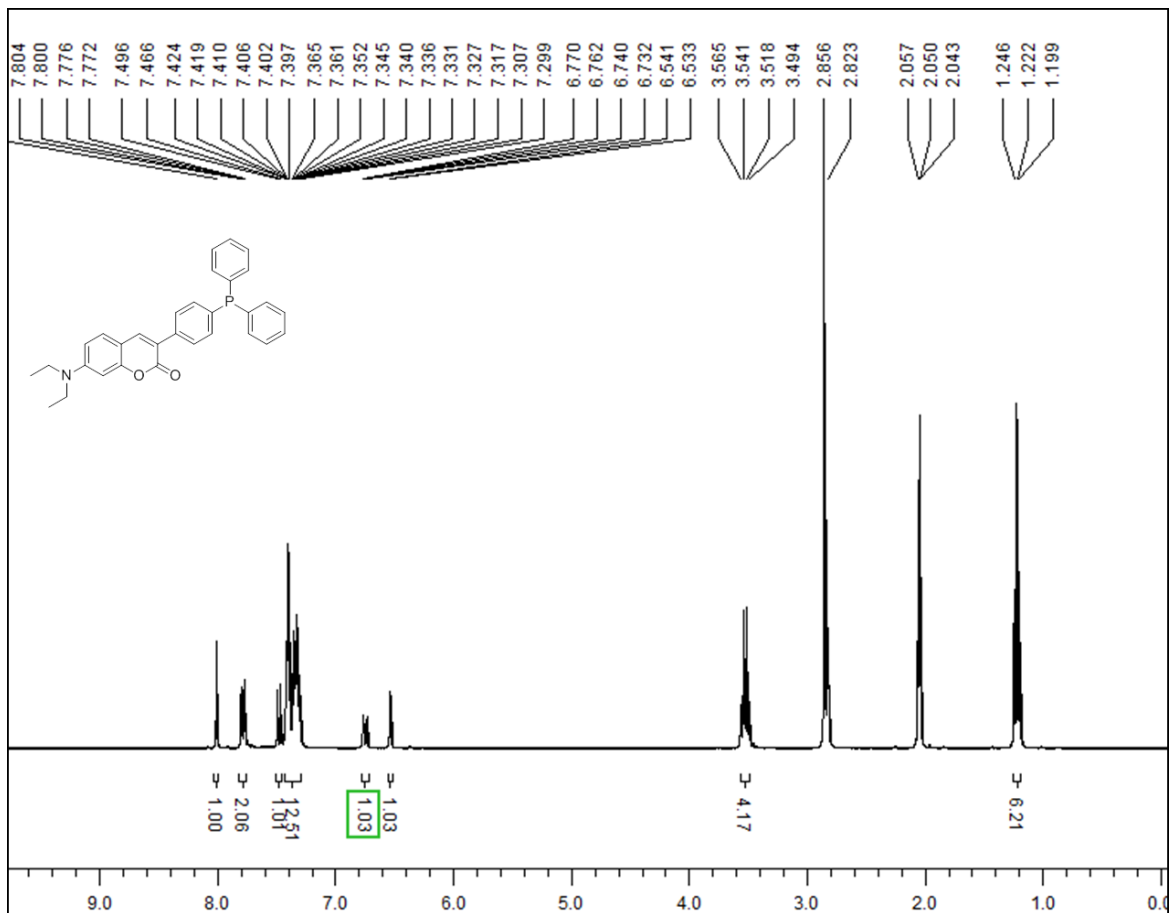
Prominent unintegrated peaks are from the NMR solvent ((CH<sub>3</sub>)<sub>2</sub>CO and H<sub>2</sub>O).

Note: Some reduced (deiodinated) material remains and was not purified further.

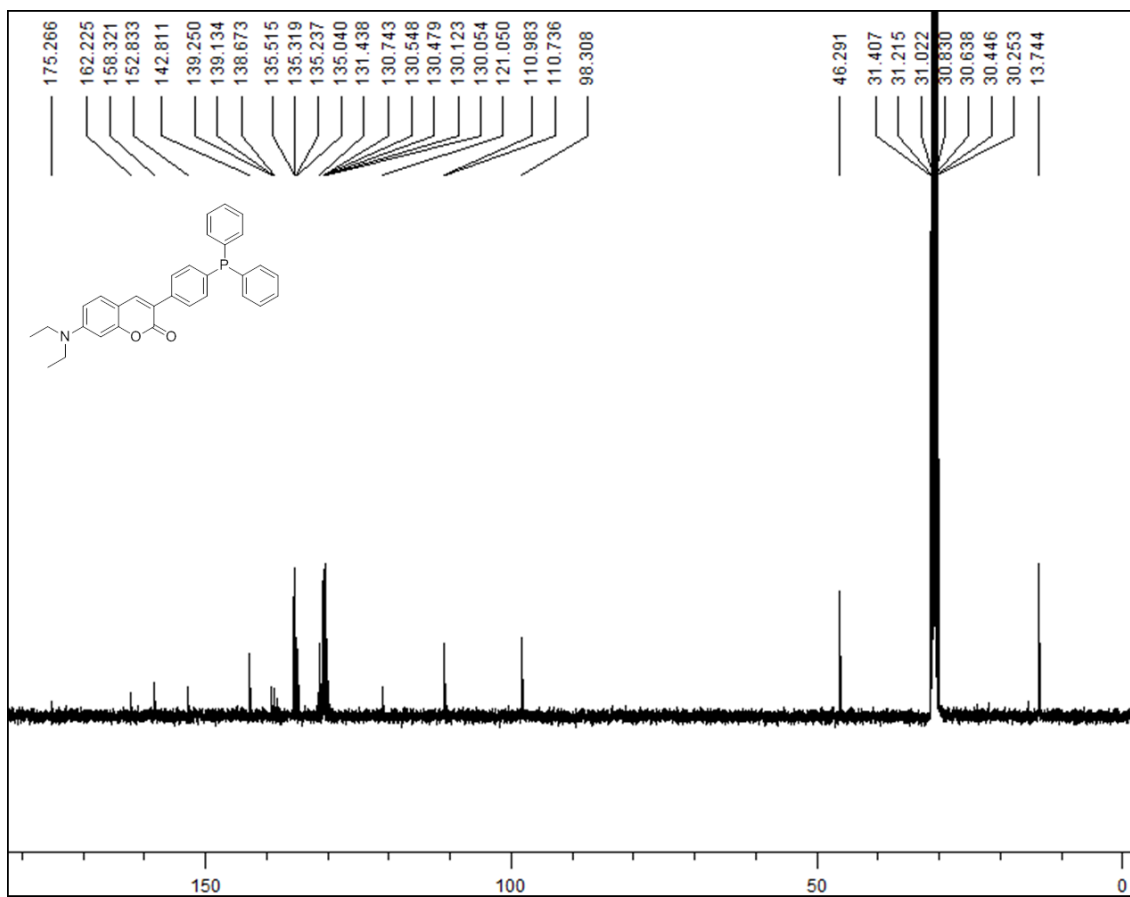


Note: Some reduced (deiodinated) material remains and was not purified further.

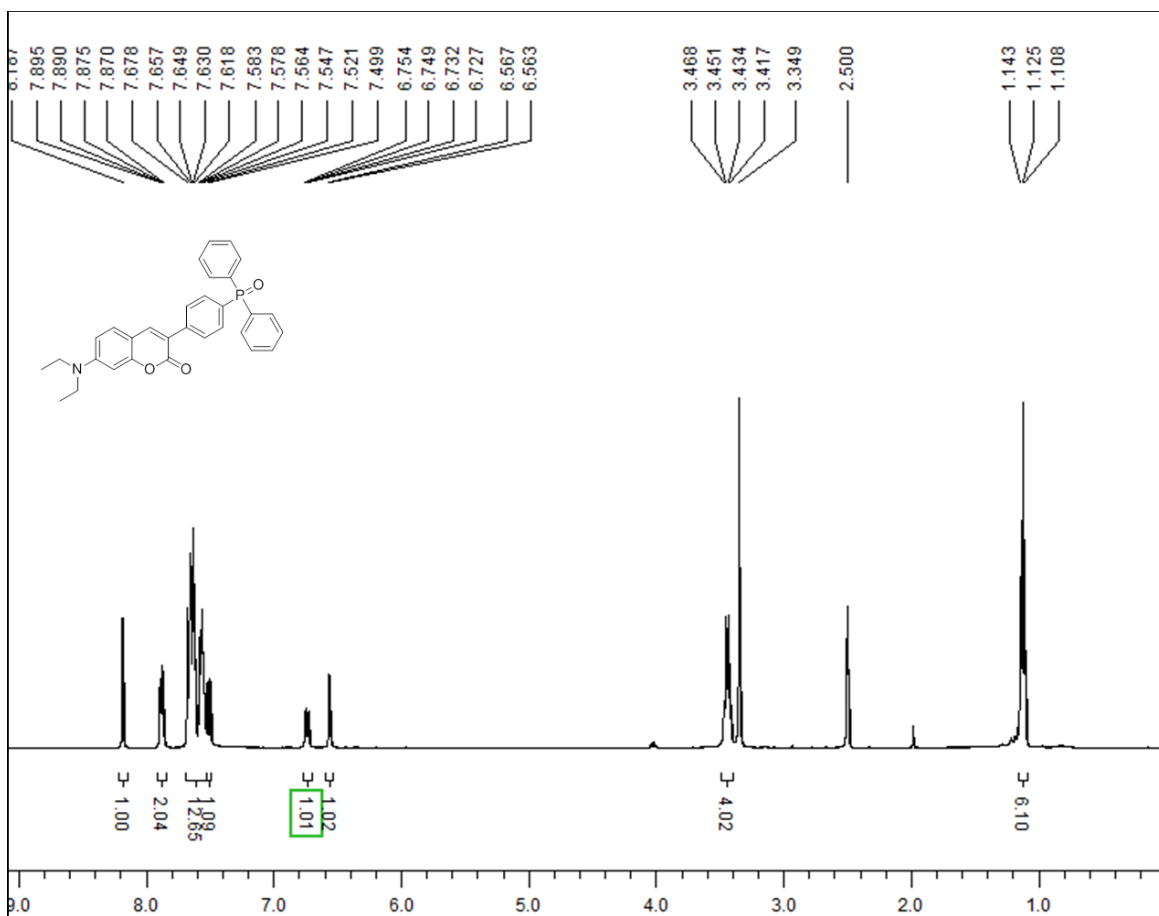
**7-(Diethylamino)-3-(4-(diphenylphosphino)phenyl)-2H-chromen-2-one (4)**



Unintegrated peaks are from the NMR solvent ((CH<sub>3</sub>)<sub>2</sub>CO and H<sub>2</sub>O).

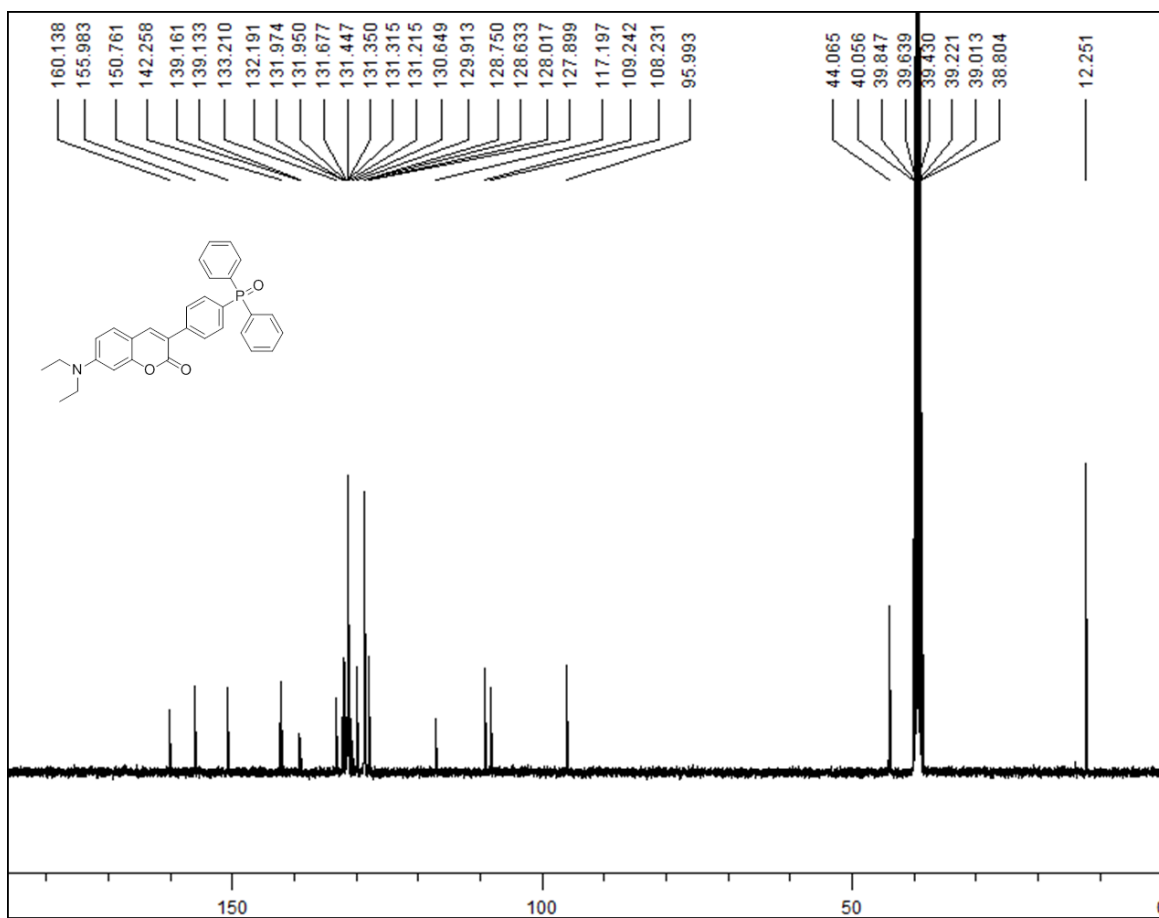


**7-(Diethylamino)-3-(4-(diphenylphosphoryl)phenyl)-2H-chromen-2-one (8)**

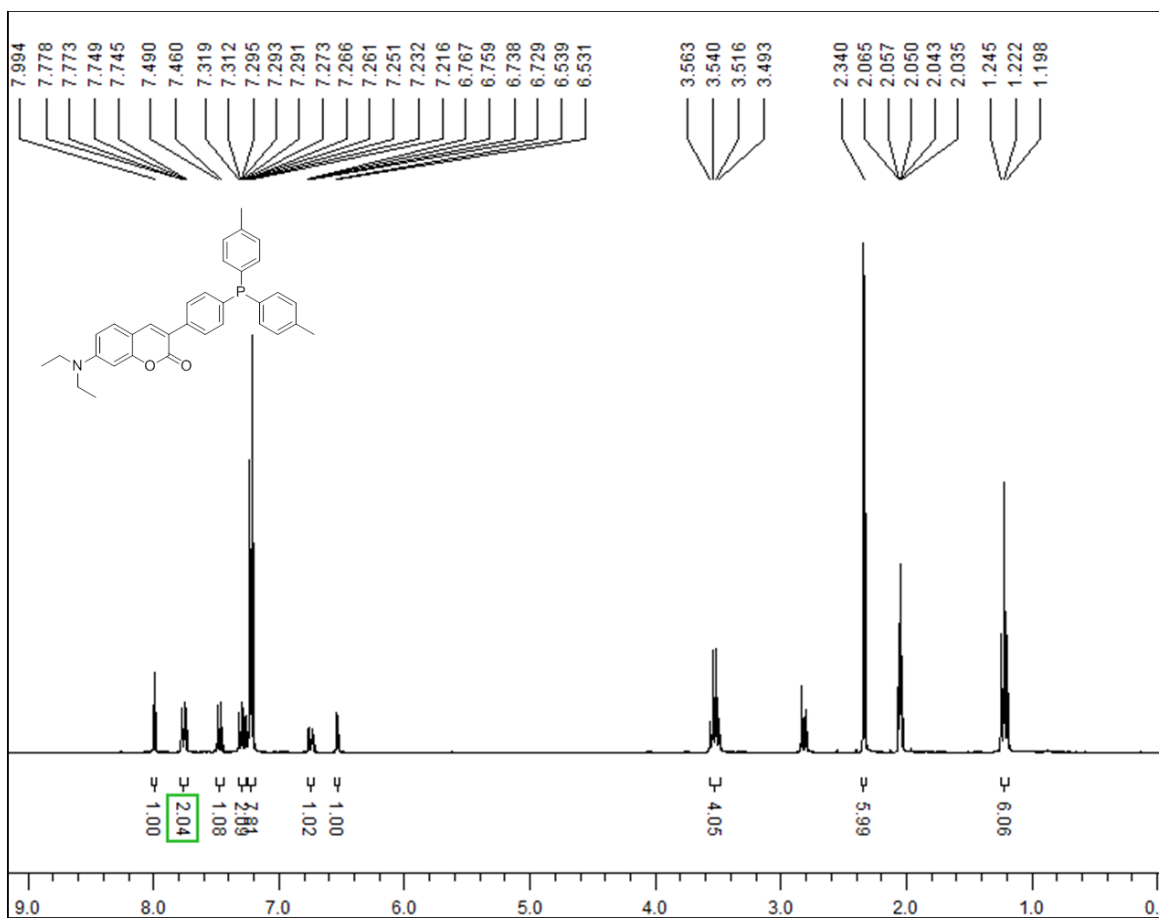


Unintegrated peaks are from the NMR solvent DMSO and H<sub>2</sub>O.

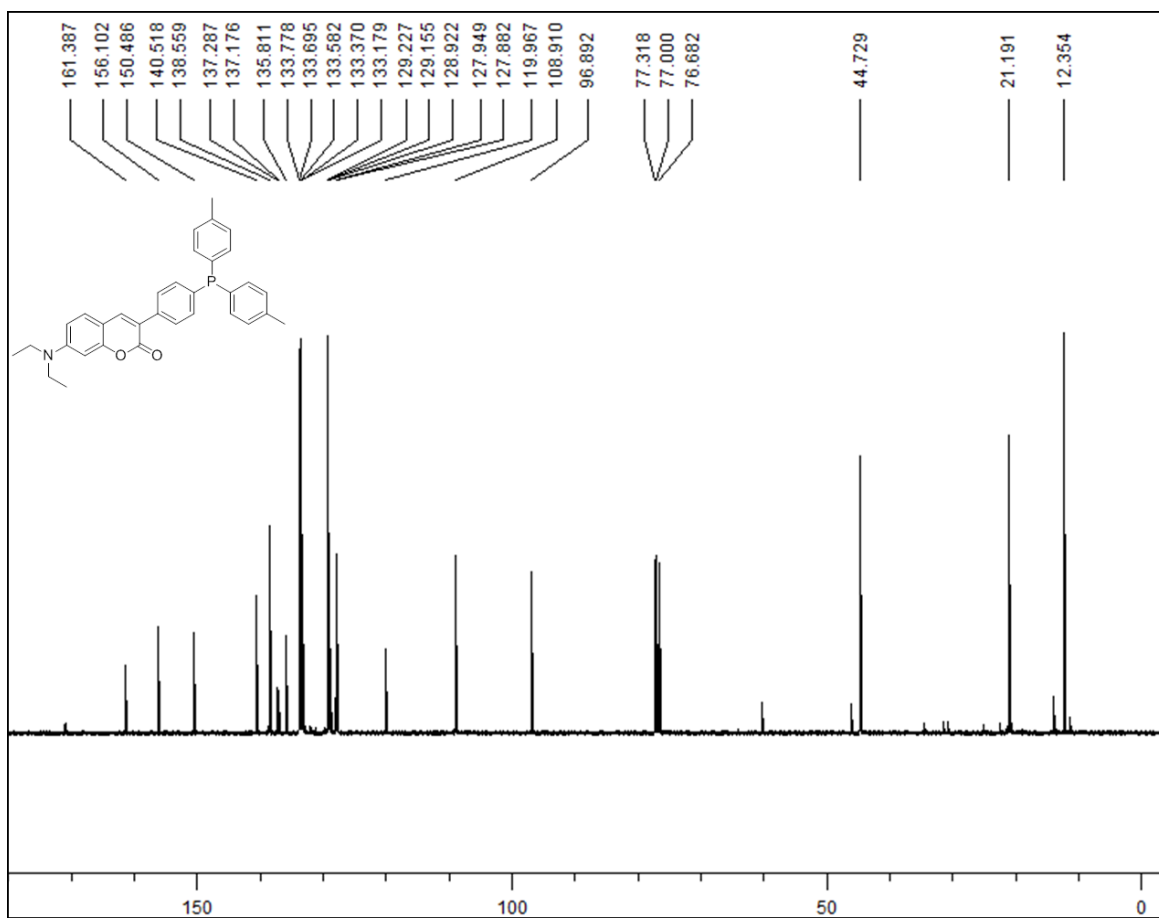




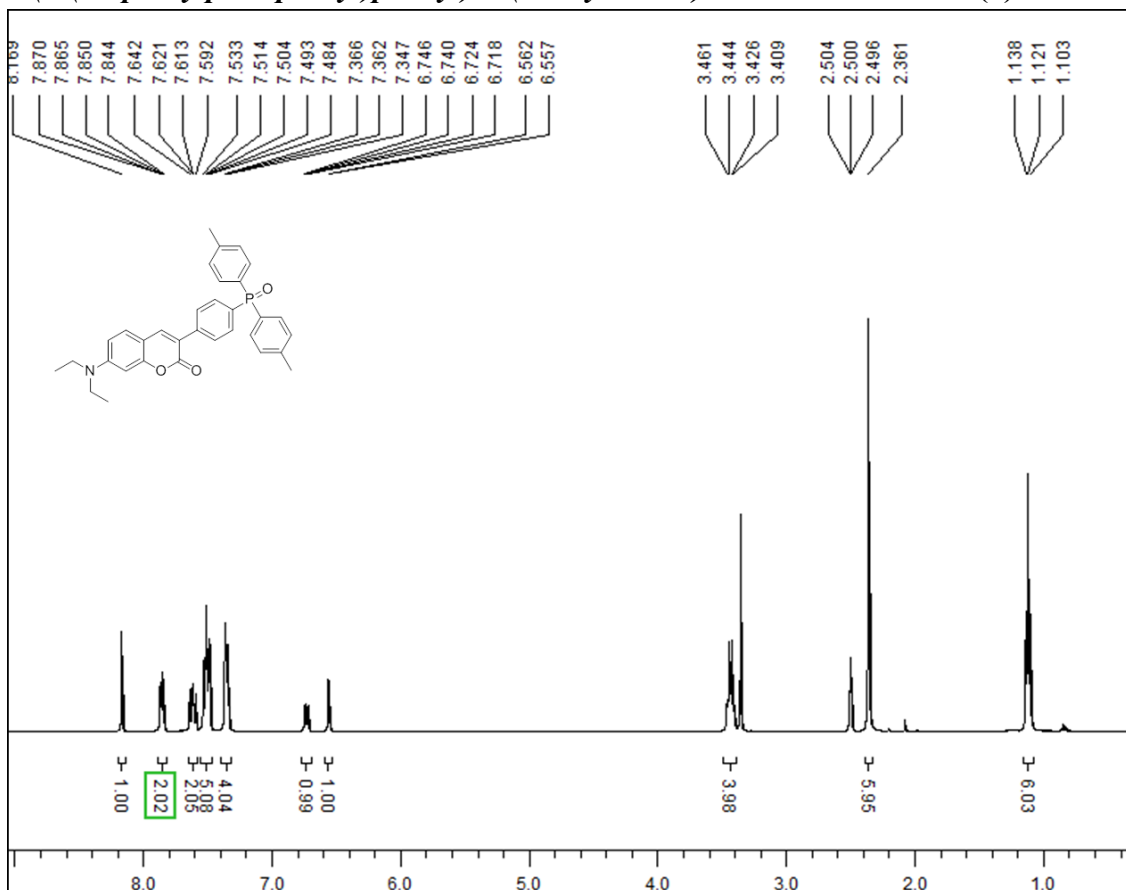
**3-(4-(Di-p-tolylphosphino)phenyl)-7-(diethylamino)-2H-chromen-2-one (5)**



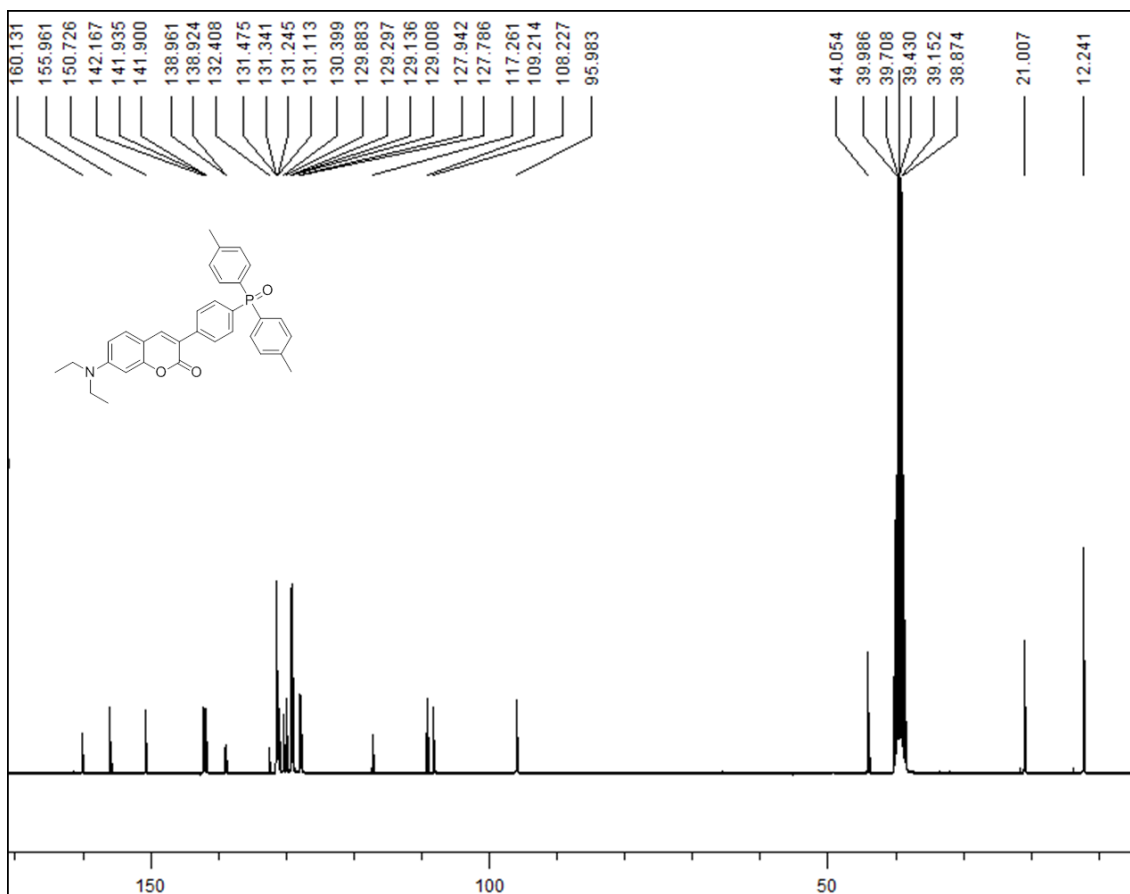
Unintegrated peaks are from the NMR solvent ((CH<sub>3</sub>)<sub>2</sub>CO and H<sub>2</sub>O).



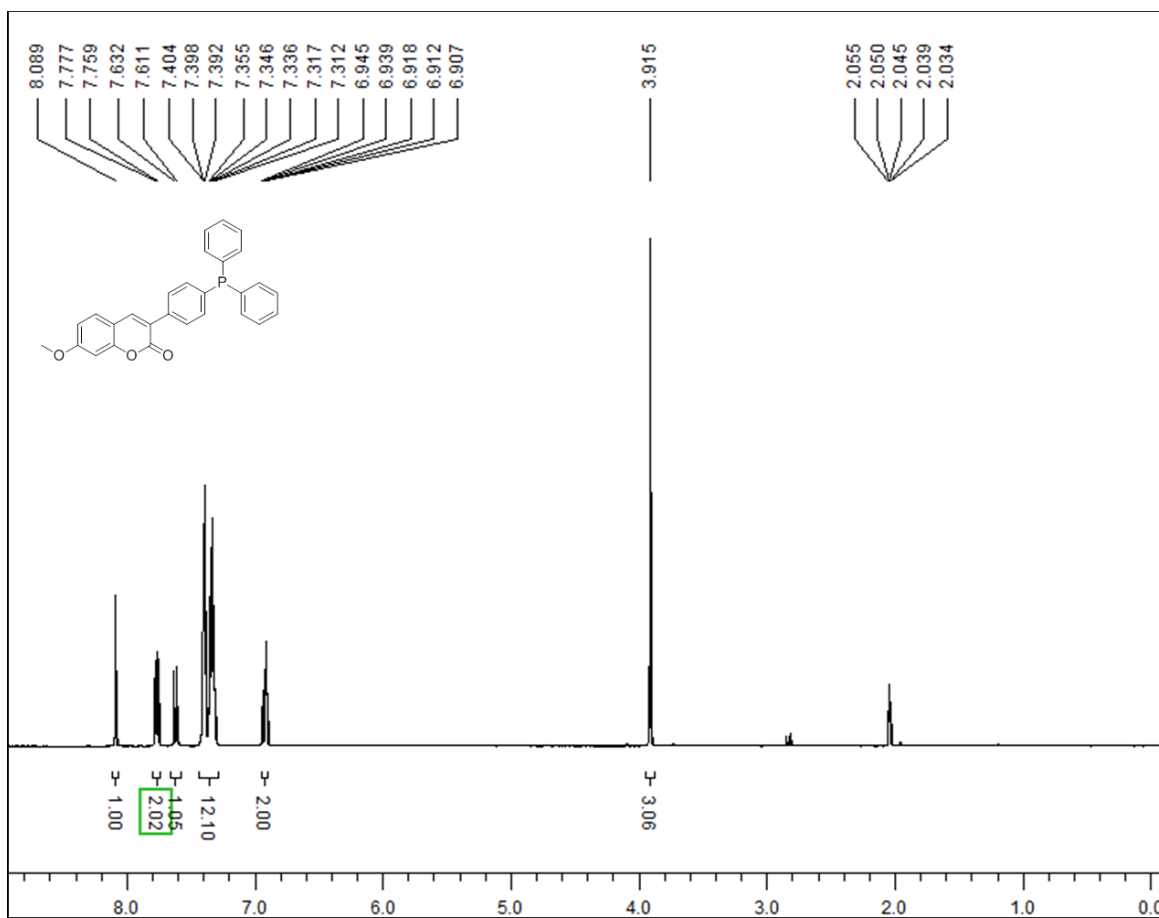
**3-(4-(Di-p-tolylphosphoryl)phenyl)phenyl)-7-(diethylamino)-2H-chromen-2-one (9)**



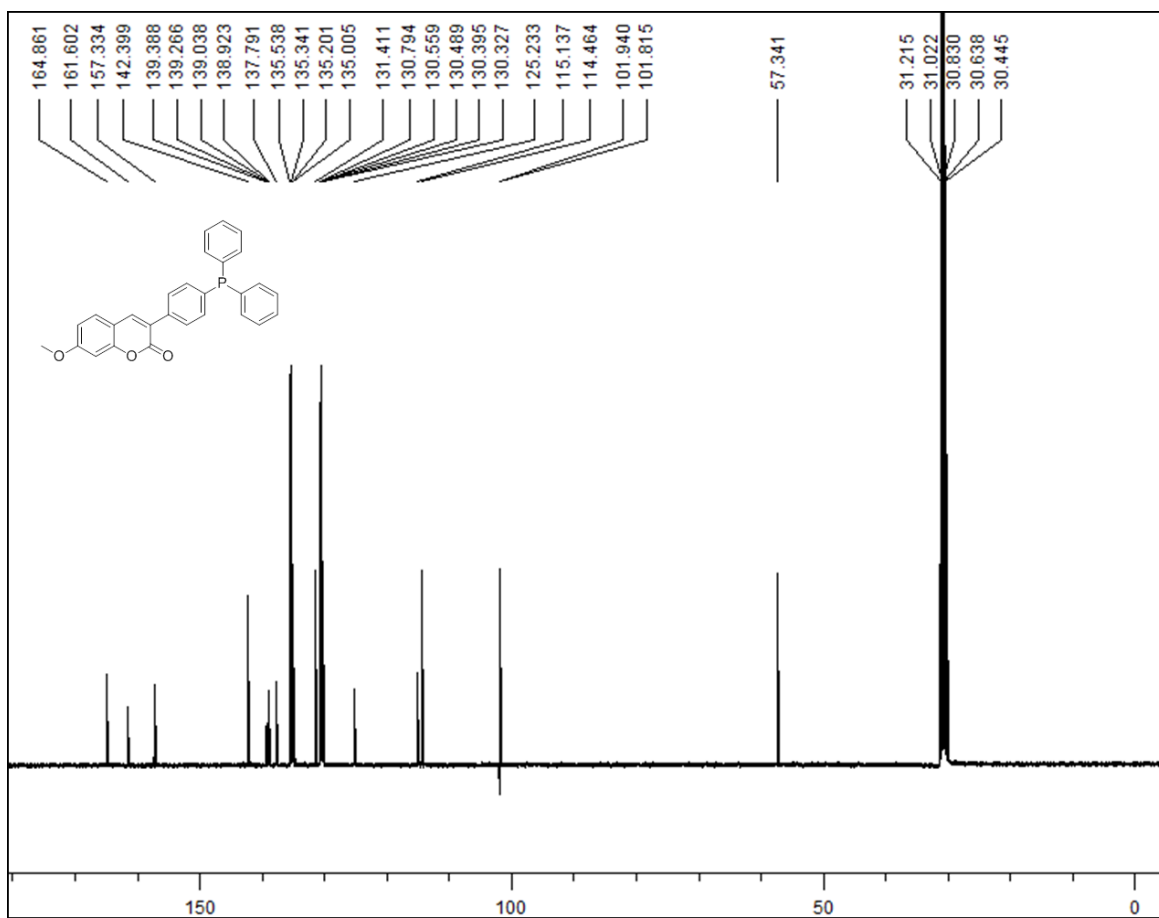
Unintegrated peaks are from the NMR solvent DMSO and H<sub>2</sub>O.



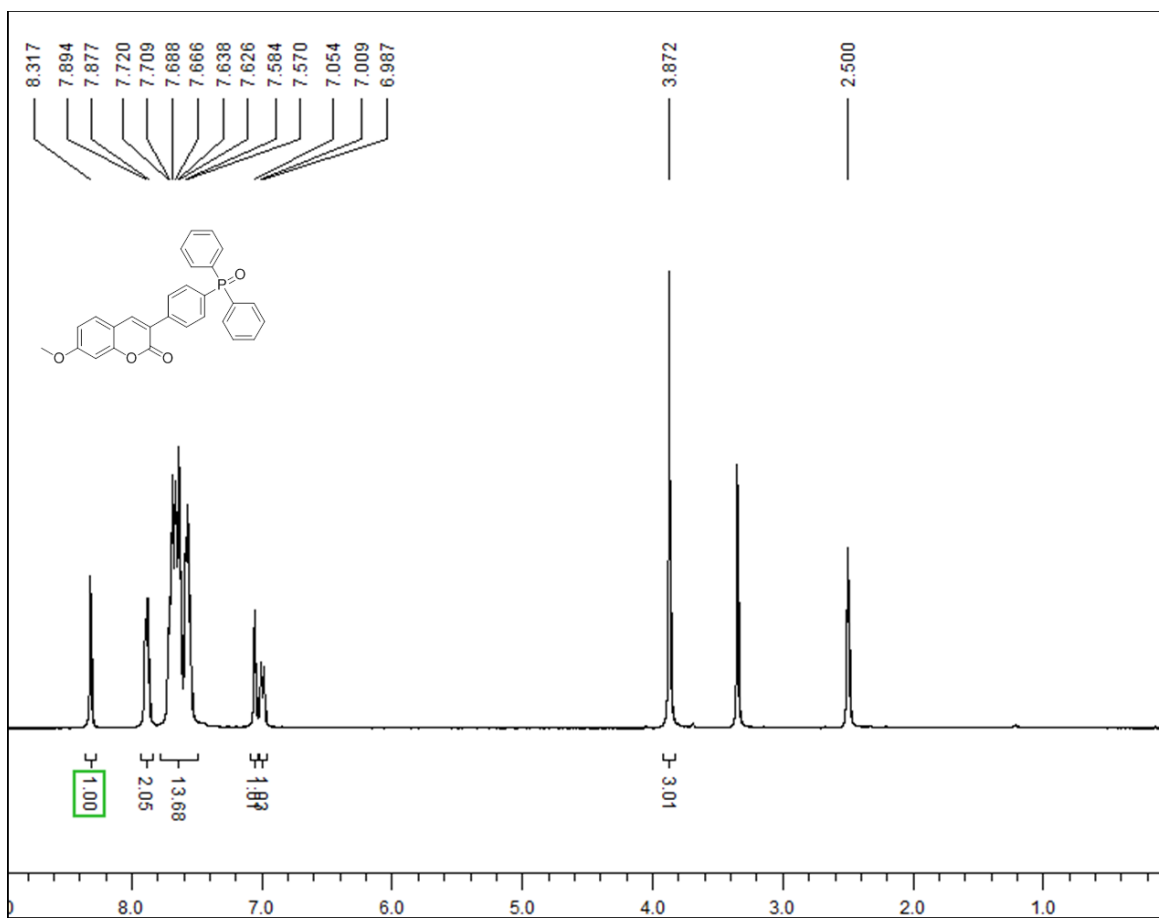
**3-(4-(Diphenylphosphino)phenyl)-7-methoxy-2H-chromen-2-one (6)**



Unintegrated peaks are from the NMR solvent (CH<sub>3</sub>)<sub>2</sub>CO and H<sub>2</sub>O.

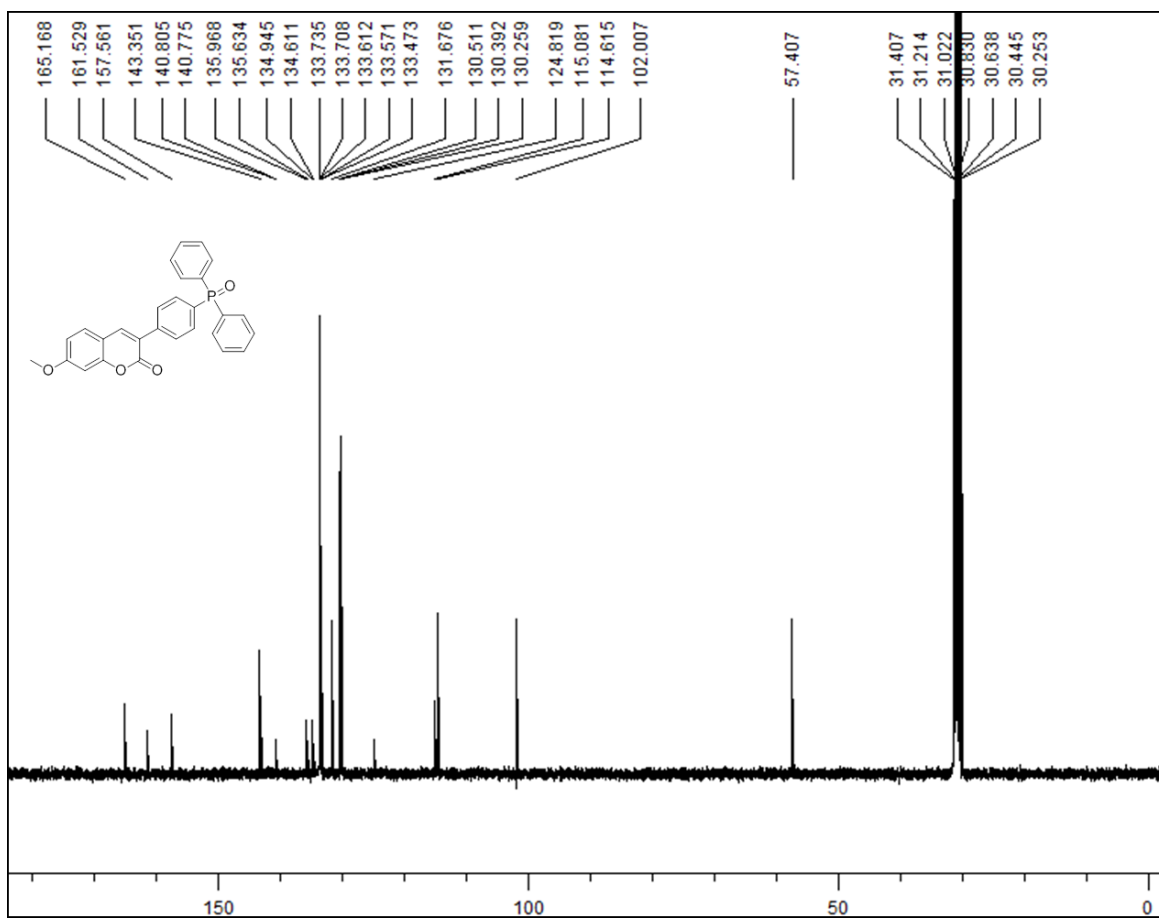


**3-(4-(Diphenylphosphoryl)phenyl)-7-methoxy-2H-chromen-2-one (10)**

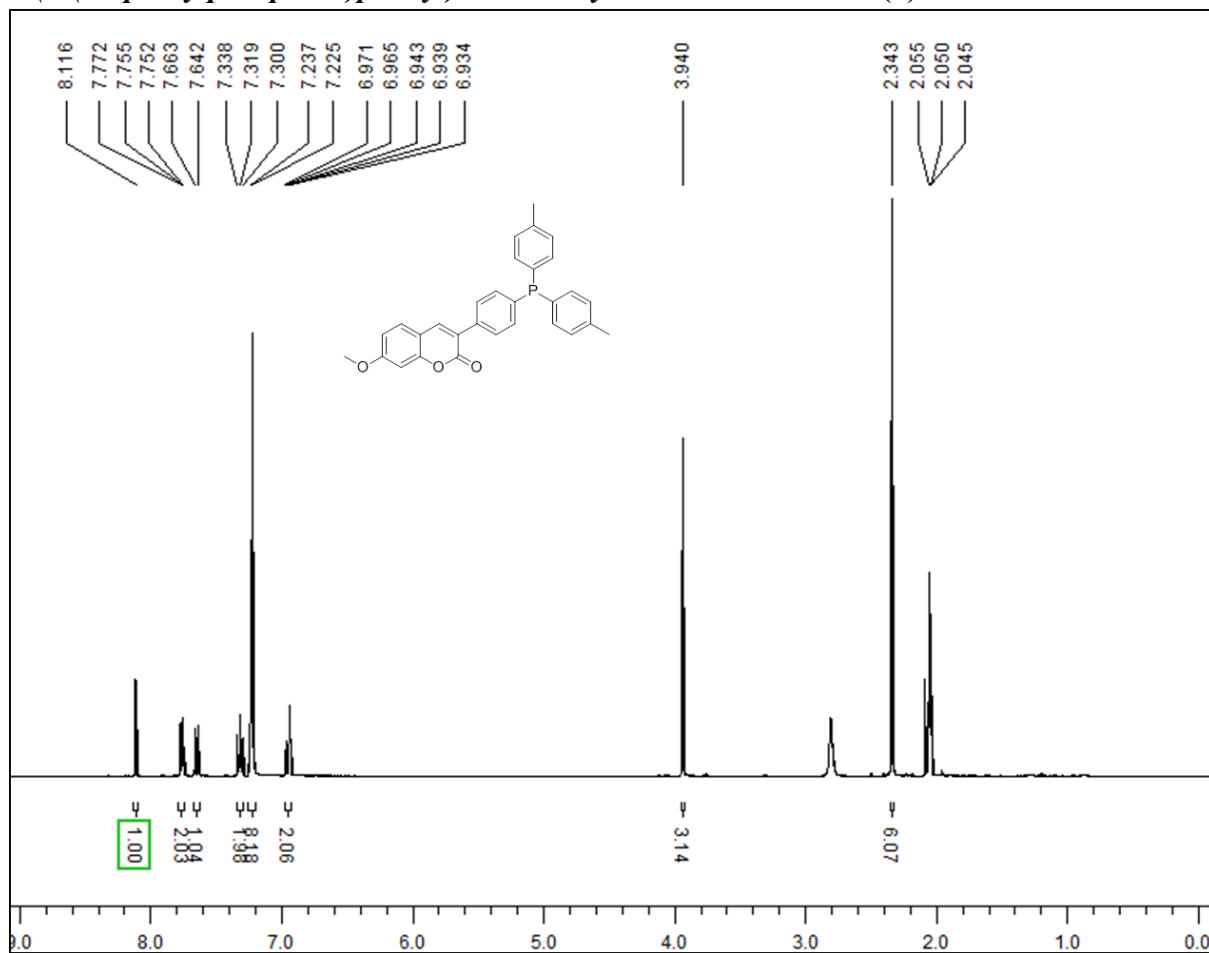


Unintegrated peaks are from the NMR solvent DMSO and H<sub>2</sub>O.

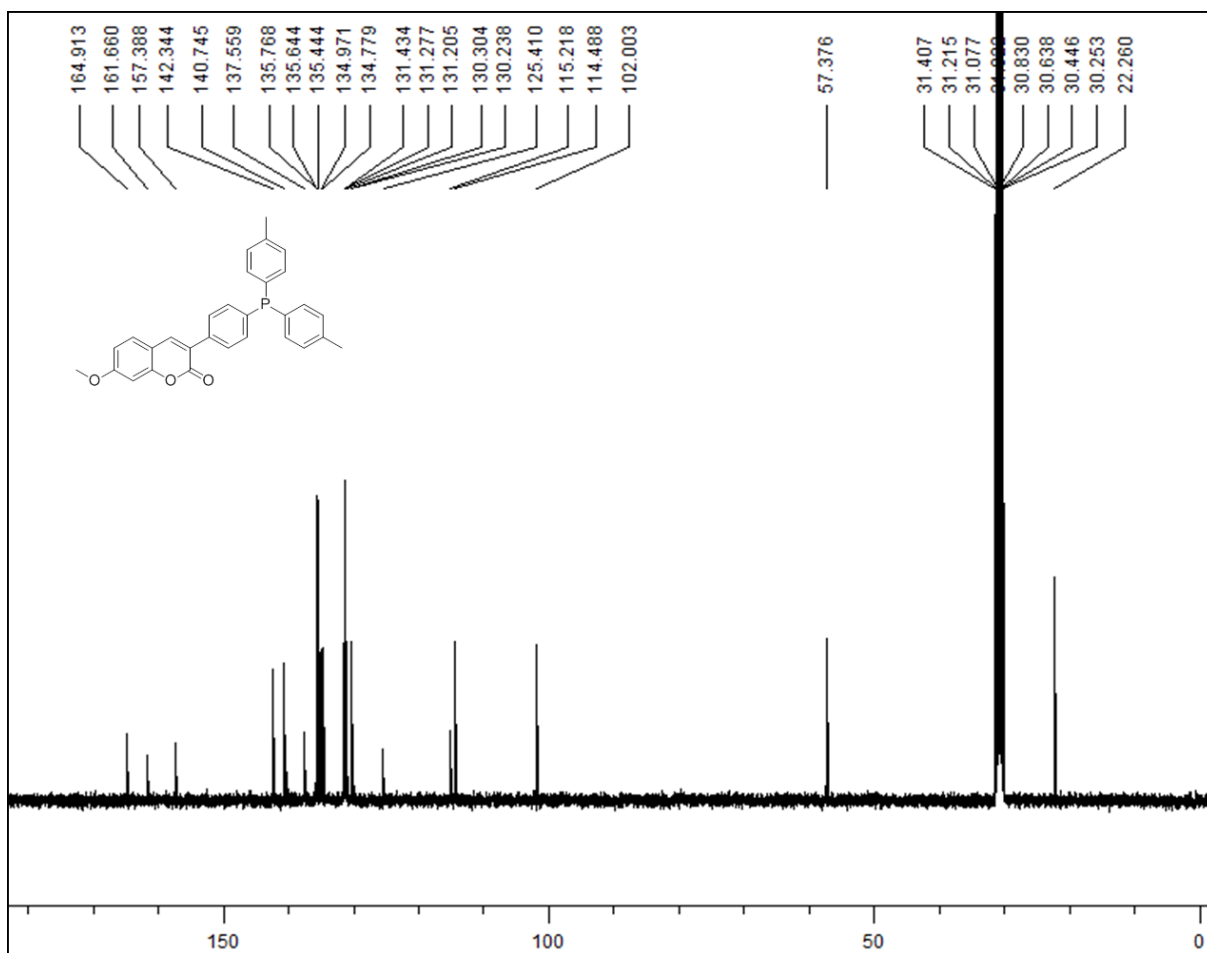




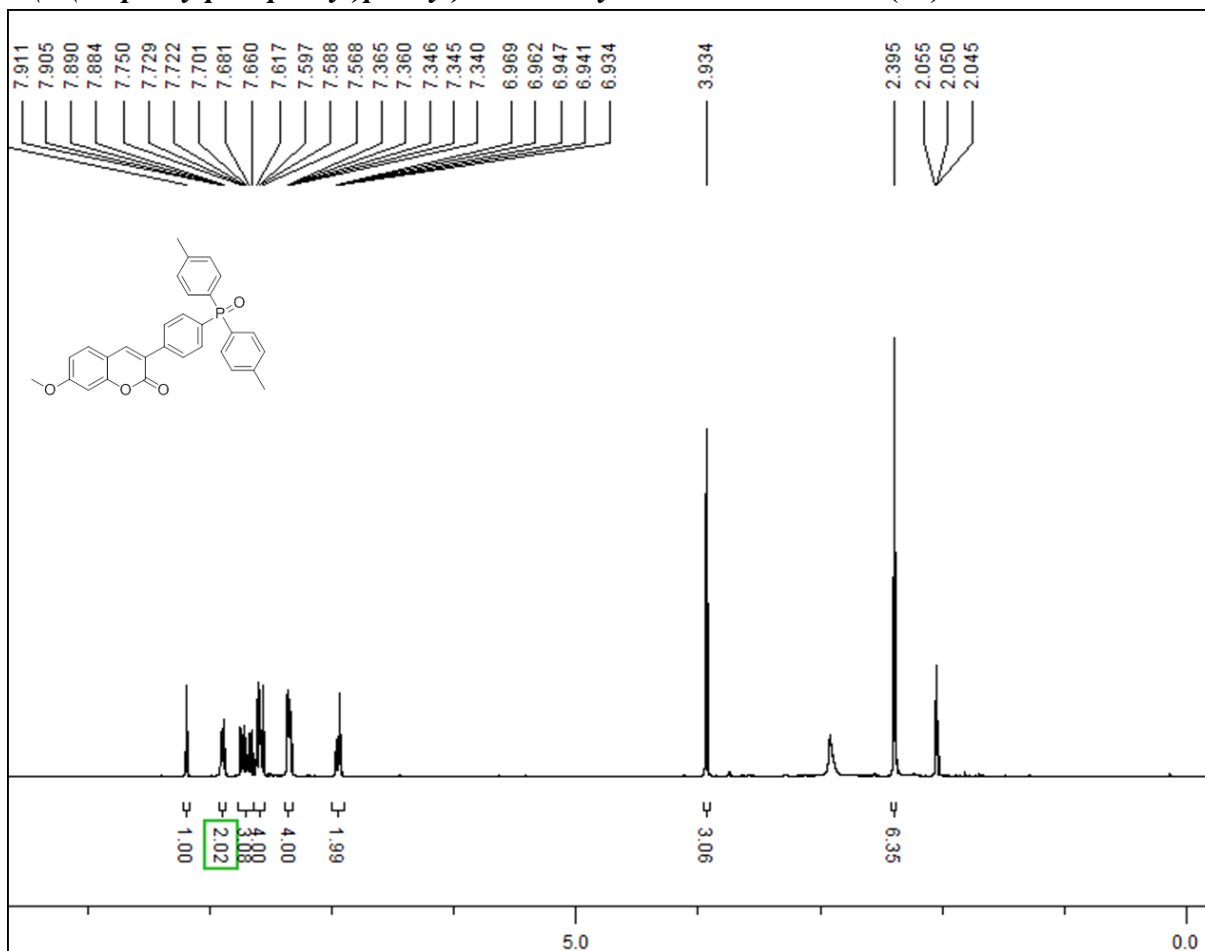
**3-(4-(Di-*p*-tolylphosphino)phenyl)-7-methoxy-2H-chromen-2-one (7)**



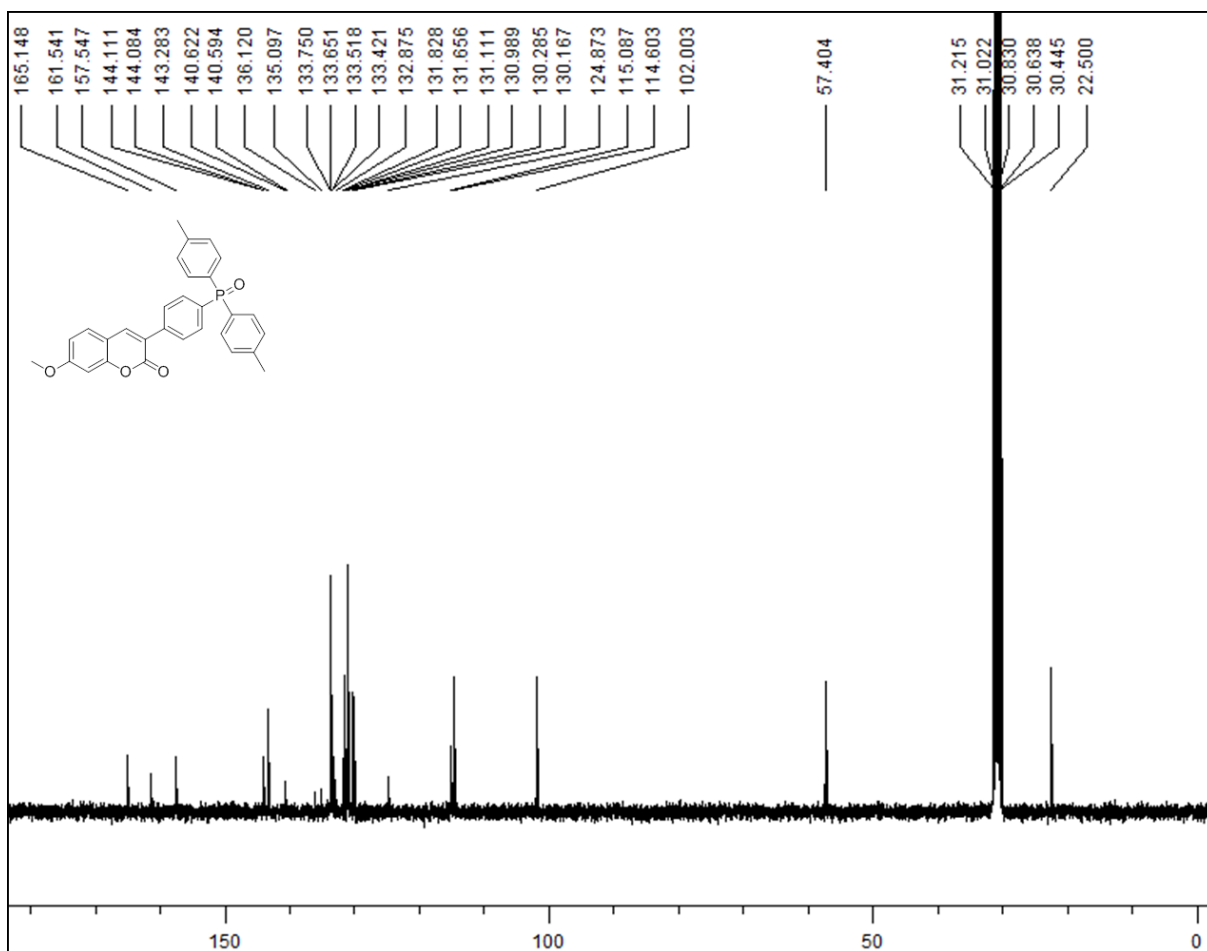
Unintegrated peaks are from the NMR solvent ((CH<sub>3</sub>)<sub>2</sub>CO and H<sub>2</sub>O).



**3-(4-(Di-p-tolylphosphoryl)phenyl)-7-methoxy-2H-chromen-2-one (11)**



Unintegrated peaks are from the NMR solvent ((CH<sub>3</sub>)<sub>2</sub>CO and H<sub>2</sub>O).



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